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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/597,636

06/02/2008

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9248-88834-US

4258

22242 7590 05/11/2011  
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EXAMINER

GABEL, GAILENE

ART UNIT

PAPER NUMBER

1641

MAIL DATE

DELIVERY MODE

05/11/2011

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/597,636	<b>Applicant(s)</b> SERTEYN ET AL.	
	<b>Examiner</b> GAILENE R. GABEL	<b>Art Unit</b> 1641	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 08 March 2011.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 15,17-24 and 26-40 is/are pending in the application.
- 4a) Of the above claim(s) 24 and 27-31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 15,17-23,26 and 32-40 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date. _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Amendment Entry***

1. Applicant's amendment and response, filed March 8, 2011, is acknowledged and has been entered. Claims 15, 17, 18, 20, 21, 26, and 36 have been amended. Claim 25 has been cancelled. Claim 40 has been added. Claims 24 and 27-31 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Accordingly, claims 15, 17-24, and 26-40 pending. Claims 15, 17-23, 26, and 32-40 are under examination.

### ***Amendment Entry***

2. Any rejections or objections not reiterated herein, have been withdrawn.
3. The rejections of claim 25 are now moot in light of Applicant's cancellation of the claim.

### **New Grounds of Rejection**

#### ***Claim Rejections – 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 26 and 37-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26, as amended, is indefinite in reciting a “kit or device ... comprising ... antibodies effective for ... and substrate effective for ...” because it is unclear how the components recited in the claim encompass a device. How do “antibodies” and “substrate” encompass a device?

Claim 26, as amended, is also indefinite in reciting, “effective” because the term “effective” is a subjective term that lacks a comparative basis for defining its metes and bounds.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 15, 17-19, 23, 26, 32, 37, and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Deby et al. (US Patent 5,460,961).

Deby et al. disclose a kit for use in immunological detection of recombinant enzyme, in this case, myeloperoxidase (MPO) and its activity, present in a biological sample containing neutrophils using enzyme-linked immunosorbent assay (ELISA). The kit comprises antibodies for immunocapturing the enzyme. The kit further comprises a chromogenic substrate effective for detecting and measuring the enzyme, wherein the chromogenic substrate may be any one of paranitrophenyl phosphate, O-dianisidine or orthophenylene diamine which transforms the enzyme into a detectable

Art Unit: 1641

reaction product. Deby et al. also teach that an effective amount of nitrite in the form of sodium salt or any other form of earth alkali salt can be added into the kit so as to enable generation of enhanced signal during measurement (col. 21, line 36 to col. 22, line 6).

Deby et al. also disclose using the kit for immunological detection of the enzyme and its enzyme activity. The enzyme present in the sample is immunocaptured using enzyme-specific antibody adsorbed onto a 96-microwell tray. Thereafter, a washing step is performed to remove unbound components which may interfere with the measurement of enzyme activity. The enzyme specific antibody may be monoclonal or polyclonal. The presence and/or amount of the enzyme is detected and measured using the chromogenic substrate used in the presence of hydrogen peroxide in the reaction mixture (col. 21, line 36 to col. 22, line 6).

As to the method in claim 15, the recitation of “for measuring the activation status of neutrophil cells” and “the sample containing the neutrophil cells and/or enzyme released by the neutrophil cells... which measures the active enzyme content only” has not been given patentable weight because the recitations occur in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Art Unit: 1641

As to the kit in claim 26, the recitation of “SIEFED”, “for measuring the activation status of neutrophil cells ... which the kit or device specifically measures the active enzyme content only” has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

In conclusion, the kit and method taught by Deby appear to be consonant to the components and method steps recited in the claimed invention. As currently recited, no difference is seen.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 20, 21, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deby et al. (US Patent 5,460,961) in view of Hansel et al. (WO 99/61907).

Deby et al. is discussed supra. Deby et al. is silent in teaching measurement and correlation of neutrophil cell activation status to a disease and/or pathology.

Hansel et al. disclose a method for measuring leucocyte enzyme activity in a biological sample (Abstract; p. 1, lines 3-8). The biological sample may be cellular or acellular such as venous or capillary blood, sputum, nasal fluids, and tissue cells (p. 10, lines 21-24). The biological sample (blood) is obtained from a mammal and contains leucocyte subpopulations including neutrophils and active enzyme released therefrom. Hansel et al. teach that the enzyme released by the leucocytes including neutrophils is MPO (Abstract; p. 1, 21-28; p. 2, lines 17-23). Hansel et al. provide that the method is effective in differentially measuring active MPO enzyme content released by the leucocytes including neutrophils, the enzyme content being correlated with leucocyte, i.e. neutrophil, cell activation status as shown in page 4, lines 5-7, page 6, lines 12-14, and page 7, lines 1-3. In the method, Hansel et al. teach contacting the enzyme MPO with hydrogen peroxide as a specific substrate and a chromogen which is transformed by active enzyme into a visible fluorimetric reaction product (p. 1, lines 9-14; p. 3, lines 7-9; p. 11, lines 21-22). The leucocyte activation status is then measured and correlated to a disease or pathological condition (Abstract). Correlation is performed by comparing the active enzyme content values with normal control samples having normal active enzyme levels from healthy subjects or mammals (p. 1, lines 21-28; p. 2, lines 10-15).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the anti-MPO antibodies as taught by Deby into the

Art Unit: 1641

method of Hansel to immunologically capture and detect active enzyme released by leucocytes including neutrophils because Deby taught application of anti-MPO antibodies for specifically binding and capturing MPO enzyme in a sample, and given that Hansel taught a method which allows differential detection and measurement of active enzymes including MPO in leucocytes, specificity requirements in accurately detecting active MPO can be enhanced by virtue of immunocapture and extraction of the specific enzyme.

7. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Deby et al. (US Patent 5,460,961) view of Deby-Dupont et al. (Equine Neutrophil Myeloperoxidase in Plasma: design of a radio-immunoassay and first results in septic pathologies, *Veterinary Immunology and Immunopathology* 66: 257-271 (1998)).

Deby et al. is discussed supra. Deby et al. differ from the instant invention in failing to teach that the mammal is a horse.

Deby-Dupont et al. teach obtaining specific antiserum against MPO and immunologically assaying for the presence and amount of MPO in horses and determining pathological conditions such as strangulation intestinal pathologies which are accompanied by local activation of neutrophils. Such conditions can be revealed by measuring tissular enzymatic activity of the granulocytic enzyme: MPO using the specific antibody (antiserum) to MPO (Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to immunologically assay for the amount and activity of enzyme MPO

Art Unit: 1641

as taught by Deby, in a blood sample obtained from a horse as taught by Deby-Dupont because Deby specifically taught that polyclonal and monoclonal antibodies can be used in immunological enzyme assay methods to specifically capture and detect accurate levels and activity of MPO from leucocytes including granulocytes and Deby-Dupont expressly showed the significance of specifically measuring accurate level and activity of MPO in determining conditions such as strangulation intestinal pathologies in horses which occurs by local activation of granulocytes, i.e. neutrophils.

8. Claims 33, 34, 38, and 39 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Deby et al. (US Patent 5,460,961) in view of Terao et al. (US Patent 5,290,679).

Deby et al. is discussed supra. Deby et al. differ from the instant invention in failing to teach that the active enzyme is elastase or trypsin.

Terao et al. teach that elastase and trypsin are granulocyte enzymes that are also released by granulocytes including neutrophils, the concentrations and enzyme activities of which are also measured immunologically. Terao et al. specifically teach measuring elastase using anti-elastase antibody conjugated to enzyme labels (Example 6 and Example 7).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to immunologically detect and measure levels and activity of other enzymes such as elastase and trypsin as taught by Terao using polyclonal or monoclonal anti-elastase antibodies and anti-trypsin antibodies in immunological

Art Unit: 1641

enzyme assays such as applied with MPO as taught by Deby because elastase and trypsin appear to be obvious variations of other active enzymes released by subpopulations of granulocytes including neutrophils when activated, as in the method of Deby.

9. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Deby et al. (US Patent 5,460,961) in view of Wilson et al. (US 2006/0257879).

Deby et al. is discussed supra. Deby et al. differ from the instant invention in failing to teach a substrate which is 10-acetyl-3,7-dihydroxyphenoxazine.

Wilson et al. teach that peroxidase activity is present in many cells and that many fluorogenic substrates for horseradish peroxidase are well known in the art and are commercially available in ELISA kits. Wilson et al. specifically teach that 10-acetyl-3,7-dihydroxyphenoxazine is a well-known fluorogenic substrate which is advantageous for its ability to react with hydrogen peroxide in the presence of horseradish peroxidase and produce highly fluorescent resolution signal.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate 10-acetyl-3,7-dihydroxyphenoxazine as a fluorogenic substrate into the method of Deby in immunologically detecting and measuring level and activity of MPO because 10-acetyl-3,7-dihydroxyphenoxazine appears to be an obvious variation of fluorogenic substrate known and used in immunological enzyme assay methods such as taught Deby, which is advantageous for its ability to produce highly fluorescent resolution signal.

***Response to Arguments***

10. Applicant's arguments filed March 8, 2011 have been fully considered but they are not persuasive.

A) Applicant argues that Deby et al. fail to teach or suggest a kit which specifically measures active enzyme product and a substrate effective for detecting and/or measuring active enzyme present and instead teach a completely different method in which a total MPO including active or inactive is immunocaptured and detected.

In response, claim 26 which is drawn to a kit recites the following components as part of the kit: "antibodies effective for immunocapturing the enzyme" and "a substrate effective for detecting active enzyme." Deby et al. teach using "mouse antihuman MPO monoclonal antibody" which appears to be an antibody effective for immunocapturing an enzyme (MPO) and a "a chromogenic substrate" which is "paranitrophenyl phosphate" which appears to be a substrate effective for detecting active enzyme" in column 21, lines 37-64 and nowhere in the claim clearly sets forth how the broadly recited "antibodies" and "substrate" are effective to immunocapture, and effective to detect active enzyme, much less active MPO, and even much less active MPO released from neutrophils, which the preamble appears to purport to. Specifically, the claimed invention recites consonant components to that taught by Deby et al. and no difference is seen.

As to the recitation "for immunocapturing the enzyme" and "for detecting active enzyme", a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

As to the recitation of "for measuring the activation status of neutrophil cells ... which the kit or device specifically measures the active enzyme content only," such limitations have not been given patentable weight because the recitations occur in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Applicant's arguments therefore fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

Accordingly, it appears that the claimed invention reads on the teaching of Deby et al. and the rejection of claims 15, 17-19, 23, 26, 32, 37, and 40, is hereby, maintained and also instated for its relevancy to newly amended claims.

B) Applicant argues that Hansel et al. does not distinguish neutrophil MPO from eosinophil MPO and other leucocytic MPOs. Applicant further contends that Hansel does not provide enabling details as to how to differentiate between measurement of MPO activity and eosinophil MPO activity. Applicant also argues that Hansel does not distinguish between the enzyme activities without a prior cell separation.

In response, claims 15, 20, and 21 to which the Hansel reference is applied in combination with Deby as the primary reference, recite "immunocapturing the enzyme with an enzyme specific ... antibody" and "detecting and/or measuring active enzyme" and in claim 20, "neutrophil cell activation status is measured" to imply but not clearly define that the enzyme is released from neutrophils; whereas nowhere in the claims clearly set forth how the broadly recited "antibodies" and "substrate" are supposedly effective to immunocapture, and effective to detect active enzyme, much less active MPO, and even much less active MPO released from neutrophils, which the preamble appears to purport to. Deby et al. is relied upon as primary reference for using "mouse antihuman MPO monoclonal antibody" which appears to be an antibody effective for immunocapturing an enzyme (MPO) and using a "chromogenic substrate" which is "paranitrophenyl phosphate" which appears to be a substrate effective for detecting active enzyme" in column 21, lines 37-64. Hansel et al. is further relied upon as a secondary reference for measuring differential leucocyte enzyme activity, i.e. active enzyme, in a biological sample, wherein the enzyme released by the leucocytes including neutrophils is MPO (Abstract; p. 1, p. 1, lines 3-8 & 21-28; p. 2, lines 17-23).

Art Unit: 1641

Specifically, the claimed invention recite consonant components and method steps to that taught by the combination of Deby et al. and Hansen et al., and no difference is seen.

As to the method in claim 15, the recitation of “for measuring the activation status of neutrophil cells” and “the sample containing the neutrophil cells and/or enzyme released by the neutrophil cells... which measures the active enzyme content only” has not been given patentable weight because the recitation occurs in the preamble and are not recited in body of the rejected claims. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Applicant's arguments therefore fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

Accordingly, it appears that the claimed invention suggests the combined teaching of Deby et al. in view of Hansel et al. suggest the claimed invention, as currently recited.

Art Unit: 1641

11. Applicant's arguments with respect to other issues and references as applied to the claims have been considered but are moot in view of the new grounds of rejection.

12. No claims are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GAIENE R. GABEL whose telephone number is (571)272-0820. The examiner can normally be reached on Monday, Tuesday, Thursday, 5:30 AM to 4:00 PM.

Art Unit: 1641

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GAILENE R. GABEL/  
Primary Examiner, Art Unit 1641

May 3, 2011